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MAY 25 1989

RECEIVED & ACKNOWLEDGED

EXAMINER	
CARSON, N	
ART UNIT	PAPER NUMBER
183	6

DATE MAILED: 05/22/89

This is a communication from the examiner in charge of your application.

COMMISSIONER OF PATENTS AND TRADEMARKS

8-1-88
11-14-88
12-19-88

[X] This application has been examined [X] Responsive to communication filed on [ ] This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), [redacted] days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. [X] Notice of References Cited by Examiner, PTO-892.
2. [X] Notice re Patent Drawing, PTO-948.
3. [X] Notice of Art Cited by Applicant, PTO-1449
4. [ ] Notice of informal Patent Application, Form PTO-152
5. [X] Information on How to Effect Drawing Changes, PTO-1474
6. [ ] _____

Part II SUMMARY OF ACTION

1. [X] Claims 1-28 are pending in the application.

   Of the above, claims _____ are withdrawn from consideration.

2. [ ] Claims _____ have been cancelled.

3. [ ] Claims _____ are allowed.

4. [X] Claims 1-28 are rejected.

5. [ ] Claims _____ are objected to.

6. [ ] Claims _____ are subject to restriction or election requirement.

7. [X] This application has been filed with informal drawings which are acceptable for examination purposes until such time as allowable subject matter is indicated.

8. [ ] Allowable subject matter having been indicated, formal drawings are required in response to this Office action.

9. [ ] The corrected or substitute drawings have been received on _____. These drawings are [ ] acceptable; [ ] not acceptable (see explanation).

10. [ ] The [ ] proposed drawing correction and/or the [ ] proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been [ ] approved by the examiner. [ ] disapproved by the examiner (see explanation).

11. [ ] The proposed drawing correction, filed _____, has been [ ] approved. [ ] disapproved (see explanation). However, the Patent and Trademark Office no longer makes drawing changes. It is now applicant's responsibility to ensure that the drawings are corrected. Corrections MUST be effected in accordance with the instructions set forth on the attached letter "INFORMATION ON HOW TO EFFECT DRAWING CHANGES", PTO-1474.

12. [ ] Acknowledgment is made of the claim for priority under 35 U.S.C. 119. The certified copy has [ ] been received [ ] not been received [ ] been filed in parent application, serial no. _____; filed on _____.

13. [ ] Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

14. [ ] Other

SN 200754

DOCKETED
Reminder July 22, 1989
Response due Aug 22, 1989
Stat Bar Nov 22, 1989

PTOL-326 (Rev. 7-82) EXAMINER'S ACTION

Applicant's are requested to amend the specification to correctly set forth the status of related applications SN 055298, pending, and SN 868585, now abandoned, and parent application SN 055229, now abandoned.

The disclosure is objected to because of the following informalities: on page 27, the third line from the bottom, the term "glycorhetinic" is incorrect; on page 41, line 10, the units designation does not appear, defining "50 Tris HCl". Appropriate correction is required.

Claim 26 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only. See MPEP 603.01(i). Accordingly, this claim has not been further treated on the merits.

Claims 1-2, 4, 13, 16, and 27 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-2 are considered indefinite in that no parameters are set forth for the reverse phase high pressure liquid chromatography (RP-HPLC) step. Separation of extract components by RP-HPLC depends upon the column used, the mobile phase, and the chromatography conditions. Mere recitation of "subjecting said extract to reverse phase high pressure liquid chromatography" fails to particularly point out and distinctly define the invention, since "RP-HPLC" merely defines a generic separation technique. It is the claim language which must particularly point out the Applicant's invention, limitations found in the specification but not in the claims are not read into the claims.

In claim 2, line 2, the term "adjuvants" should be "adjuvant" to be consistent with the method of obtaining "a substantially pure saponin".

In claims 4 and 13, the column length should have a space therein, namely "25 cmL" should be "25 cm L".

In claims 16 and 27, recitation of "other than QA-7, QA-17, QA-18, or QA-21" renders said claim indefinite since such does not set forth the "substantially pure saponin" of Applicant's invention, but merely sets forth that which the "substantially pure saponin" is not. As stated above, it is the claim language which must particularly point out and distinctly claim that which Applicant regards as the invention. The instant claim language, directed to a "substantially pure saponin" which is not QA-7, QA-17, QA-18, or QA-21, fails to point out what the "substantially pure saponin" does comprise.

In addition, claims 16 and 27 are considered indefinite in reciting, "by the method in Examples 3 and 4", since is it unclear what that method is. What "Examples 3 and 4" are intended? The specification can not be relied upon for limitations not set forth in the claims.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

"A person shall be entitled to a patent unless -

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States."

The following is a quotation of 35 U.S.C. 103 which forms the basis for all obviousness rejections set forth in this Office action:

> "A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior

art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person."

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

Claims 1-3 are rejected under 35 U.S.C. § 102 (b) as being anticipated by each of Combier et al (4335113), Toyo Jozo (54-132218), Kishimoto Sangyo (61-7286), Nagasawa et al (Chem. Pharm. Bull. 28:2059-2064), or Zhou et al (Chem. Pharm. Bull. 29:2844-2850).

Each of the references disclose methods of obtaining substantially pure saponins comprising the same steps as those set forth in the instant claims.

Claims 4-28 are rejected under 35 U.S.C. 103 as being unpatentable over Higuchi et al (Phytochemistry 26:229-235) or Scott et al (Int. Archs. Allergy Appl. Immun. 77:409-412) in combination with Combier et al, Toyo Jozo, Kishimoto Sangyo, Nagasawa et al, or Zhou et al, as set forth above.

Each of Higuchi et al and Scott et al teach the mixture of saponin adjuvants in the bark extract of *Quillaja* species. That said extract contains a mixture of saponins is well known.

Applicant's claims are directed to substantially pure saponins and pharmaceutical compositions containing such. The prior art references differ, at best, from the instant claims in the specific recitation of QA-7, QA-17, QA-18, and QA-21. It would have been obvious to one of ordinary skill in the art to substantially purify the conventional saponin adjuvant mixture of Scott et al or Higuchi et al, known to enhance the immune response to antigen, since purification of various saponins is well known and advantageous, as disclosed by each of the secondary references.

Saponin adjuvants are generally known, together with pharmaceutical compositions containing antigen and saponin. Claims to "substantially pure saponin adjuvant" are not considered patentable over the prior art saponin adjuvant, since a difference in purity is merely a matter of degree, unless the pure product has a different, unobvious utility. Substantially pure saponins are well known as seen in the secondary references. Application of such disclosures to the saponin adjuvant mixture of Higuchi et al or Scott et al would have been obvious to the worker in the art to obtain the expected pure saponin having fewer impurities and being less toxic.

Claims 16-20 and 27 are rejected under 35 U.S.C. § 102 (b) as being anticipated by Dalsgaard (Archiv fur die gesamte Virusforschung 44:243-254).

The Dalsgaard reference discloses a purified saponin adjuvant which is less toxic than crude *Quillaja* extract. In addition, Dalsgaard teaches employing said saponin adjuvant in a pharmaceutical composition together with an antigen, to induce the production of antibodies to said antigen, thereby enhancing the immune response. Such a disclosure anticipates the instant claims.

Claims 18-28 are rejected under 35 U.S.C. 103 as being unpatentable over Dalsgaard (as cited above), Nunberg (4789702), Freidrich-Loeffler (DL 0160763), or Buchnev (SU 0548046).

Each of the references disclose the known combination of saponin adjuvant and various antigens in pharmaceutical compositions. Selection of any known saponin adjuvant for combination with antigen, in compositions as disclosed would be within the purview of the skilled artisan.

No claim is allowed.

The Sakuma et al (J. Chromatog. 400:293-295) reference is cited of interest.

An inquiry concerning this communication should be directed to Nancy Carson at telephone number (703) 557-0664.

NSC 5/16/89

Ronald W. Griffin

RONALD W. GRIFFIN
PRIMARY EXAMINER
ART UNIT 183